



## CHAPTER 6

### CONCLUSION

Based on the hypothesis that GABA/BzR complex and its ligands involve in the pathogenesis of HE, this randomized double-blind clinical trial was conducted to demonstrate the effectiveness of a specific BzR antagonist, flumazenil, in the fast improvement of the impaired mental status of cirrhotic patients with HE and to observe their long-term outcomes of these patients.

After 1 mg flumazenil was injected intravenously, 8 out of 13 patients in the treatment group showed positive responses of different degrees, while only one patient in the control group (1/12, with placebo -- normal saline) showed such reaction, but much more lately. Statistically significant difference was found for this positive response between these 2 groups. Such positive reaction to flumazenil could happen in HE patients in any stages and with rarely severe adverse effects. However, among the responders, only 3 in the treatment initiated effectively their improvement fast and could almost maintain the improved HE stages up to

the nearly normal stages (stage 0 or 1) for the whole observation period. Though none in the placebo group had such obvious improvement, there was no statistical significance between the 2 groups. However the power was not strong enough. The duration of these positive responses of most patients was not long and unstable. Most of the patients in both groups regained their relatively normal mental function in the following 2nd to 5th day. There was no difference of the unfavorable mortality (about 1/3) between these 2 groups.

From the results of this study, it can be concluded as the following: Flumazenil can improve the mental status of a part of cirrhotic patients with hepatic encephalopathy (about 60%). This improvement initiates rapidly comparing to the other conventional therapies, but lasts short. It does not change or have any effect on the survival of these patients. Because of the small sample size in this study, the effect of individual characteristics could not be overlooked. Well-designed, multicenter study with large samples including the economic analysis is necessary to further evaluate the therapeutic position of flumazenil via different intaken routes in the management of HE. So far, it should be prudent in offering this compound

unselectively to the HE patients of any stages. It seems rational to try to apply this agent to those patients who do not show any response to the conventional therapies in order to achieve the purpose that the other drugs could not achieve. The willingness to pay of the family members should be considered for a desperate patient.



ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย